

# Long-Term Antibiotic Cost Savings from a Comprehensive Intervention Program in a Medical Department of a University-Affiliated Teaching Hospital

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**We tested a low-cost, multifaceted intervention program comprising formulary restriction measures, continued comprehensive education, and guidelines to improve in-hospital use of antibiotics and related costs. In a short-term analysis, total antibiotic consumption per patient admitted, which was expressed as defined daily doses (DDD), decreased by 36% ( $P < .001$ ), and intravenous DDDs decreased by 46% ( $P < .01$ ). Overall expenditures for antibiotic treatment decreased by 53% (US\$100 per patient admitted). The 2 main cost-lowering factors were a reduction in prescription of antibiotics (35% fewer treatments;  $P < .0001$ ) and more diligent use of 5 broad-spectrum antibiotics (23% vs. 10% of treatments;  $P = .001$ ). Quality of care was not compromised. A pharmacy-based, prospective, long-term surveillance of DDDs and costs over 4 years showed an ongoing effect. This comprehensive intervention program, which aimed to reduce antibiotic consumption and costs, was highly successful and had long-lasting effects.**

Antibiotics may account for up to 30% of a hospital's drug budget [1–3]. For many years, inappropriate use of antibiotics has been recognized as a major problem and a reason for high costs, as well as the selection and spread of drug-resistant microorganisms [4–7]. Various strategies have been used to implement guidelines and antimicrobial-control programs to reduce costs and limit the emergence and spread of antimicrobial-resistant organisms [8, 9]. Strategies include education, formulary restriction (i.e., mandatory approval of certain restricted antibiotics by clinical pharmacists or infectious diseases specialists), pharmacy justification, for-

mulary substitution, early switch from intravenous to oral delivery, computer surveillance, and multidisciplinary approaches [9]. Cost-saving effects were demonstrated in several studies [3, 10–22], but, with a one exception [15], the duration of follow-up was mostly short (<2 years). Most studies dealt with interdisciplinary interventions performed at large medical centers [3, 10, 12, 13, 17–22], where hospital staff made decisions about antibiotic use in direct or indirect interaction with clinical pharmacists and infectious diseases specialists or with the help of computer decision-support systems [14, 15]. However, smaller hospitals with less sophisticated computer systems may face difficulties in implementing programs like these [15].

We developed a multifaceted intervention program in response to a steady increase in the use and costs of antibiotics in our department since 1992. Our program combines several well-known methods, such as broad education, guidelines, formulary restriction, special approval for certain restricted drugs, and early switches from intravenous to oral therapy. The program

Received 9 April 2003; accepted 17 September 2003; electronically published 13 January 2004.

Financial support: Santésuisse; the Gottfried and Julia Bangerter-Rhyner Foundation.

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**Clinical Infectious Diseases** 2004;38:348–56

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1058-4838/2004/3803-0006\$15.00

was continuously enforced over a period of 4 years and was designed to particularly address the needs of a medical department in a small-sized teaching hospital. The objective of the present study was 2-fold: to evaluate the short-term effect of the program on costs and clinical outcomes in individual patients, and to monitor the long-term effect on costs on the basis of data provided by the hospital pharmacy in the years after the implementation of the program.

## PATIENTS AND METHODS

**Setting.** The Department of Internal Medicine of the Kantonsspital Schaffhausen, Switzerland, is a tertiary care center with 80 beds and the only hospital in a region of ~80,000 inhabitants. Thus, patients are nonselected and the disease spectrum is broad. The staff of the department consists of 13 residents in general internal medicine, who usually rotate every 2 years, and 5 staff physicians and attendants with a specialty in general internal medicine. The department admits ~2200 patients per year.

**Study design.** This is a quasi-experimental study, with chart review of 500 consecutive patients admitted in the period before and after implementation of the program. Use of antibiotics and their costs, as documented in pharmacy records, were analyzed in the 4 years after implementation of the program.

**Patients.** For the short-term analysis, we analyzed 500 consecutive patients admitted after full implementation of the program by 1 January 1998 and compared these with 500 consecutive patients admitted in 1997 (i.e., the last group of patients who were admitted before the program was initiated). All patients aged  $\geq 18$  years who were admitted to the general wards or the intensive care unit (ICU) and who stayed in hospital for  $>24$  h were included. There were no exclusions.

Every patient admitted to the Department of Internal Medicine was included in the prospective, pharmacy-based 4-year follow-up study of antibiotic expenditures. Costs for patients admitted to the ICU were analyzed separately because the hospital pharmacy could not distinguish medical from nonmedical patients, with the former making up two-thirds of the ICU population. Therefore, costs for ICU patients are based on those for medical and surgical patients, but the latter are not part of the intervention program.

**Intervention.** The antimicrobial formulary was reevaluated, judged to be reasonable, and left unchanged. Mandatory approval by a staff physician for restricted drugs (ceftriaxone [with the exception of its use for the treatment of meningitis], ceftazidime, piperacillin-tazobactam, imipenem-cilastatin, and vancomycin) had been introduced several years earlier and was reinforced. A comprehensive educational program and written guidelines were established. We introduced the intervention

program in a stepwise manner starting in May 1997, with full implementation by the end of 1997. The head of the department (S.R.) was responsible for implementation, maintenance, continuous surveillance, and outcome evaluation.

The education program comprised the following:

- Provision of the latest antimicrobial cost data and presentation of the intended intervention program to the medical staff.
- Lecture on appropriate use of antimicrobial drugs, with special emphasis on the avoidance of unnecessary treatments.
- Instruction on the indications for a priori oral application of an antibiotic or for a switch from intravenous to oral delivery as early as possible.
- Lectures on clinical presentation, diagnosis, and treatment of the most important and most frequent infectious diseases.
- Weekly rounds with the medical staff on every ward to evaluate antimicrobial treatments on the basis of the guidelines, as outlined below.
- Regular feedback every 6 months to the medical staff regarding antimicrobial expenditures.
- Regular yearly provision of hospital antimicrobial susceptibility patterns.

In addition, written guidelines were established on (1) the appropriateness of empirical antimicrobial treatment, including a checklist to be considered before start of therapy; (2) the appropriate choice of antibiotics during the empirical phase, and once culture results and susceptibility patterns of the causative organism were known; and (3) the route of delivery, dosing, and duration of treatment for the most important infections. Recommendations were based on the severity of disease, the most likely causative organisms, and their resistance pattern at our hospital. The guidelines are accessible for each physician in a personal booklet and on the hospital's internal Web site. They are modified by the responsible physician whenever necessary, and changes are immediately communicated to the medical staff. The head of the department advised the medical team to follow the guidelines, but patient care and choice of antibiotics were left to the discretion of the treating physicians.

**Quality assessment.** We included the following parameters to measure the overall quality of care provided before and after implementation of the program: overall in-hospital survival, reasons for death, in-hospital clinical improvement or cure of patients treated with antibiotics, duration of hospital stay for all patients and for those treated with antimicrobial drugs, the number of patients who experienced a relapse during the hospital stay, and the rehospitalization rate within 30 days after discharge.

**Data collection.** The following data were abstracted by one of the authors (B.K.) from the medical charts of the 1000 patients: age, sex, principal diagnosis, infectious disease diagnosis, length of hospital stay, and cause of death. Additional

**Table 1. Characteristics of patients and conditions leading to antimicrobial treatment before and after establishment of the intervention program.**

| Characteristic                                    | Before<br>intervention<br>(n = 500) | After<br>intervention<br>(n = 500) | P      |
|---|-------------------------------------|------------------------------------|--------|
| Age, mean years $\pm$ SD                          | 67 $\pm$ 17                         | 66 $\pm$ 18                        | ...    |
| Sex   |                                     |                                    | ...    |
| Male  | 254                                 | 270                                |        |
| Female  | 246                                 | 230                                |        |
| Principal diagnosis <sup>a</sup>                  |                                     |                                    |        |
| Cardiovascular disease                            | 113 (23)                            | 136 (27)                           | ...    |
| Infectious disease                                | 85 (17)                             | 57 (11)                            | ...    |
| Cerebrovascular or other neurological disease     | 66 (13)                             | 61 (12)                            | ...    |
| Cancer  | 54 (11)                             | 59 (12)                            | ...    |
| Gastrointestinal disease                          | 50 (10)                             | 57 (11)                            | ...    |
| Lung disease                                      | 50 (10)                             | 35 (7)                             | ...    |
| Neuropsychiatric disease                          | 27 (5)                              | 34 (7)                             | ...    |
| Other   | 55 (11)                             | 51 (10)                            | ...    |
| Conditions leading to prescription of antibiotics | 232 (46)                            | 148 (30)                           | <.0001 |
| Respiratory tract infection                       | 109 (22)                            | 72 (14)                            | .002   |
| Urinary tract infection                           | 46 (9)                              | 32 (6)                             | .01    |
| Gastrointestinal and abdominal infection          | 29 (6)                              | 6 (1)                              | .0001  |
| Fever and suspected bacterial infection           | 20 (4)                              | 16 (3)                             | .50    |
| Cellulitis  | 13 (3)                              | 10 (2)                             | .53    |
| Other <sup>b</sup>                                | 15 (3)                              | 12 (2)                             | .56    |
| C-reactive protein level <sup>c</sup>             |                                     |                                    |        |
| Highest, mean mg/L (range)                        | 122 (<10–582)                       | 159 (<10–588)                      | ...    |
| >250 mg/L   | 27 (11.6)                           | 32 (21.6)                          | .01    |
| >300 mg/L   | 12 (5.2)                            | 21 (14.2)                          | .002   |
| Length of hospital stay, days                     |                                     |                                    |        |
| All patients                                      |                                     |                                    |        |
| Median (range)                                    | 11 (1–110)                          | 9 (1–87)                           | ...    |
| Mean $\pm$ SD                                     | 13.8 $\pm$ 12.4                     | 12.4 $\pm$ 12.2                    | ...    |
| Treated patients                                  |                                     |                                    |        |
| Median (range)                                    | 13 (1–110)                          | 12 (1–87)                          | ...    |
| Mean $\pm$ SD                                     | 16.8 $\pm$ 15.1                     | 17.5 $\pm$ 16.4                    | ...    |

**NOTE.** Data are no. (%) of patients, unless otherwise indicated.

<sup>a</sup> As noted in the charts at the time of discharge from the hospital.

<sup>b</sup> Sepsis, meningitis, endocarditis, or prophylaxis of endocarditis.

<sup>c</sup> In patients treated with antibiotics; normal level, <5 mg/L.

data were collected for patients who received  $\geq 1$  dose of an antibiotic: name, dosage, duration, and route of administration, including timing for intravenous to oral switch for each antibiotic delivered, diagnosis leading to antibiotic treatment, success of antibiotic therapy (defined as clinical improvement, allowing withdrawal from therapy or discharge from the hospital), continuation of antibiotic therapy after discharge, and reasons for rehospitalization in the month after discharge. Susceptibility patterns of bacterial organisms were regularly followed by our Division of Infection Control.

**Statistical analysis.** The consumption of antibiotics is pre-

sented as number of defined daily doses (DDDs) [23]. Drug costs are based on public prices in Switzerland and were converted to US dollars (1CHF = US\$0.67). Drug prices remained constant for the drugs in question during the entire study period and were thus not updated according to the Consumer Price Index, which remained flat during 1996–2001 (overall increase, 4.4%). Cost calculations for nurses' workloads for intravenous treatment are based on a standardized system of workload measure (LEP; LEP AG) and on the usual wages in Switzerland. We calculated the following summary measures: (1) sum of intravenous and oral DDDs, and (2) sum of anti-

**Table 2. Defined daily doses (DDDs) of antibiotics delivered.**

| Variable  | No. of DDDs            |                       | Difference,<br>% | P    |
|---|------------------------|-----------------------|------------------|------|
|   | Before<br>intervention | After<br>intervention |                  |      |
| All patients                                      |                        |                       |                  |      |
| Total   | 2126                   | 1359                  | −36              | .001 |
| Intravenous therapy                               | 797                    | 427                   | −46              | .01  |
| Oral therapy                                      | 1329                   | 932                   | −30              | .01  |
| Per patient admitted <sup>a</sup>                 |                        |                       |                  |      |
| Mean total  | 4.3                    | 2.7                   | −36              | .001 |
| Intravenous therapy                               | 1.6                    | 0.8                   | −46              | .01  |
| Oral therapy                                      | 2.7                    | 1.9                   | −30              | .01  |
| Per patient treated <sup>b</sup>                  |                        |                       |                  |      |
| Mean total  | 9.2                    | 9.2                   | 0                | .99  |
| Intravenous therapy                               | 3.4                    | 2.9                   | −15              | .45  |
| Oral therapy                                      | 5.8                    | 6.3                   | +9               | .35  |
| Per 1000 hospital-days, all patients <sup>c</sup> |                        |                       |                  |      |
| Mean total  | 307                    | 219                   | −29              | .01  |
| Intravenous therapy                               | 115                    | 69                    | −40              | .01  |
| Oral therapy                                      | 192                    | 150                   | −22              | .13  |
| Per 1000 treatment-days <sup>d</sup>              |                        |                       |                  |      |
| Mean total  | 546                    | 525                   | −4               | .30  |
| Intravenous therapy                               | 205                    | 165                   | −20              | .41  |
| Oral therapy                                      | 342                    | 360                   | +5               | .52  |

<sup>a</sup> Data are for 500 patients.

<sup>b</sup> Before intervention, 232 patients; after intervention, 148 patients.

<sup>c</sup> Before intervention, 6914 days; after intervention, 6203 days.

<sup>d</sup> Before intervention, 3891 days; after intervention, 2589 days.

biotic drug costs. Average DDDs and costs were calculated: (1) per patient admitted, (2) per patient treated, (3) per 1000 hospital-days, and (4) per 1000 treatment-days. DDDs and costs were also calculated separately for intravenously and orally delivered antibiotics. Costs for nurses' workload, for intravenous solutions, and for the infusion equipment were added to the total drug costs.

The  $\chi^2$  test was used for comparison of categorical variables. Student's *t* test was performed for continuous variables. For all analyses, we used 2-sided tests. Analysis was performed by SAS software, version 8.2 (SAS Institute).

## RESULTS

**Patient characteristics.** The 2 groups were comparable with respect to age, sex distribution, and principal diagnosis (table 1). The length of hospital stay was shorter in the intervention group, but no difference could be observed among those patients who received antibiotic treatment. The mean highest C-reactive protein level and the proportion of patients with C-reactive protein levels of >250 mg/L and >300 mg/L before the intervention were lower than after the intervention, pointing to more severe infections in patients in the intervention period.

**Antibiotic use and cost.** Fewer antibiotic treatment courses

were administered after the implementation of the program: 232 (46%) of 500 patients were treated with  $\geq 1$  dose of antibiotic before the program, compared with 148 (30%) after the intervention ( $P < .0001$ ). There was generally a proportionate decrease in the number of conditions requiring antibiotic treatment (table 1). For example, a separate analysis of patients with upper respiratory tract infections revealed that, after the intervention, antibiotics were withheld significantly more often than before the intervention (47% vs. 24%;  $P = .04$ ).

There was a marked decrease of overall antibiotic consumption after the intervention (table 2), which translated into a 56% reduction of costs for antibiotic drugs. Intravenous drugs accounted for >90% of cost savings (table 3). Total DDDs per patient treated with antimicrobial drugs and per 1000 treatment days did not change; nevertheless, costs were reduced by approximately one-third as a result of a reduction in the use of intravenous drugs.

We observed a strong decrease in the delivery of the broad-spectrum antibiotics ciprofloxacin, ceftriaxone, imipenem-cilastatin, piperacillin-tazobactam, and ceftazidime, which were used by 54 patients (23% of treatments) and 15 patients (10%;  $P = .001$ ) before and after the implementation of the program, respectively. Total DDDs for these drugs decreased from 365

**Table 3. Costs for antibiotics delivered.**

| Variable  | Cost, US\$             |                       | Difference,<br>% |
|---|------------------------|-----------------------|------------------|
|   | Before<br>intervention | After<br>intervention |                  |
| All patients                                      |                        |                       |                  |
| Total   | 67,883                 | 29,814                | −56              |
| Intravenous therapy                               | 58,782                 | 23,264                | −60              |
| Oral therapy                                      | 9101                   | 6551                  | −28              |
| Per patient admitted <sup>a</sup>                 |                        |                       |                  |
| Mean total  | 135.8                  | 59.6                  | −56              |
| Intravenous therapy                               | 117.3                  | 46.5                  | −60              |
| Oral therapy                                      | 18.2                   | 13.1                  | −28              |
| Per patient treated <sup>b</sup>                  |                        |                       |                  |
| Mean total  | 292.6                  | 201.5                 | −31              |
| Intravenous therapy                               | 253.4                  | 157.2                 | −38              |
| Oral therapy                                      | 39.2                   | 44.3                  | +13              |
| Per 1000 hospital-days, all patients <sup>c</sup> |                        |                       |                  |
| Mean total  | 9818                   | 4806                  | −51              |
| Intravenous therapy                               | 8502                   | 3751                  | −56              |
| Oral therapy                                      | 1316                   | 1057                  | −20              |
| Per 1000 treatment-days <sup>d</sup>              |                        |                       |                  |
| Mean total  | 17,446                 | 11,515                | −34              |
| Intravenous therapy                               | 15,108                 | 8986                  | −48              |
| Oral therapy                                      | 2339                   | 2530                  | +9               |

<sup>a</sup> Data are for 500 patients.

<sup>b</sup> Before intervention, 232 patients; after intervention, 148 patients.

<sup>c</sup> Before intervention, 6914 days, after intervention, 6203 days.

<sup>d</sup> Before intervention, 3891 days; after intervention, 2589 days.

to 104, which saved US\$27,340, or 72% of the total drug cost reduction. Decreases were also noted for other antibiotics (amoxicillin, clarithromycin, metronidazole, cefuroxime, flucloxacillin, aminoglycosides, rifampin, and vancomycin), whereas the use of amoxicillin-clavulanate, penicillin, doxycycline, and trimethoprim-sulfamethoxazole increased. No other antibiotics were used.

Inclusion of nonantibiotic drug costs (i.e., workload, infusion equipment, and drip solutions) for intravenous treatment

(US\$32.27 per intravenous DDD) translated into additional total costs of US\$25,722 for the preintervention and US\$13,780 for the postintervention group. Total expenditures for antimicrobial therapy decreased by >50% with inclusion of these costs (table 4).

**Characteristics of antimicrobial treatment.** In general, although the difference was not statistically significant, antibiotics were administered more frequently orally (45% vs. 49%) and less frequently by intravenous delivery alone (29% vs. 24%).

**Table 4. Drug-associated plus non-drug-associated costs of antimicrobial treatment.**

| Variable                             | Cost, US\$             |                       | Difference,<br>US\$ (%) |
|--------------------------------------|------------------------|-----------------------|-------------------------|
|                                      | Before<br>intervention | After<br>intervention |                         |
| All patients                         | 93,605                 | 43,595                | 50,010 (−53)            |
| Per patient <sup>a</sup>             | 187.3                  | 87.1                  | 100.2 (−53)             |
| Per patient treated                  | 403.5                  | 294.6                 | 108.9 (−27)             |
| Per 1000 hospital-days, all patients | 13,538                 | 7028                  | 6510 (−48)              |
| Per 1000 treatment-days              | 24,057                 | 16,838                | 7219 (−30)              |

<sup>a</sup> Data are for 500 patients.

**Table 5. Outcome assessment of study groups.**

| Outcome parameter   | Before intervention | After intervention | P   |
|---|---------------------|--------------------|-----|
| Mortality   |                     |                    |     |
| Overall   | 49/500 (9.8)        | 42/500 (8.4)       | .44 |
| Patients treated with antibiotics   | 38/232 (16.4)       | 28/148 (18.9)      | .52 |
| Patients treated with antibiotics who died of infection                         | 18/38 (47)          | 12/28 (43)         | .72 |
| Patients without antibiotics  | 11/268 (4.1)        | 14/352 (4.0)       | .94 |
| Patients without antibiotics who died of infection                              | 2/11 (18)           | 0/14 (0)           | .18 |
| Total infection-related mortality   | 20/500 (4.0)        | 12/500 (2.4)       | .15 |
| Cure or improvement   | 194/232 (84)        | 120/148 (81)       | .52 |
| Relapse during hospital stay  | 4/232 (1.7)         | 2/148 (1.4)        | .72 |
| Length of stay, median, days  |                     |                    |     |
| All patients  | 11                  | 9                  |     |
| Antibiotic-treated patients   | 13                  | 12                 |     |
| Percentage of patients discharged from the hospital while receiving antibiotics | 40.6                | 39.5               | .84 |
| Rehospitalization rate  |                     |                    |     |
| Total   | 40/500 (8.0)        | 43/500 (8.6)       | .60 |
| Due to infection (relapse included)   | 9/500 (1.8)         | 5/500 (1.0)        | .28 |
| Relapse   | 4/232 (1.7)         | 1/148 (0.7)        | .65 |

**NOTE.** Data are n/N (%), unless otherwise indicated.

Switches from intravenous to oral antibiotic use were performed equally often (26% vs. 27%) and occurred in both groups after a median of 3.0 days. The mean number of antibiotics per patient (1.4) was identical in both groups, and in-hospital treatment duration was 1 day shorter after the intervention (median, 8.0 vs. 7.0 days). The percentage of patients who completed the antibiotic treatment regimen after discharge from the hospital was identical (40.6% and 39.5%).

**Outcome of antimicrobial treatment.** Overall mortality did not change after the intervention, whereas the infectious disease-specific mortality rate decreased from 4.0% to 2.4% (table 5). The percentages of patients with clinical improvement and cure were similar in both observation periods. Relapses during the hospital stay or after discharge and necessitating readmittance were slightly less frequent after the intervention. The overall rehospitalization rate was the same in both groups. In patients who needed rehospitalization, there was no hint of infections that had been missed during the previous hospital stay.

**Costs of development, implementation, and maintenance of the program.** No new positions were created for setting up and maintaining the program, nor were any other activities curtailed. The development of the guidelines in 1997 required, in total, ~200 h. The implementation of the program through lectures and weekly rounds in 1997 required ~350 h for the whole medical staff. The maintenance of the project (i.e., lectures, rounds, and revision of guidelines), required ~500–600

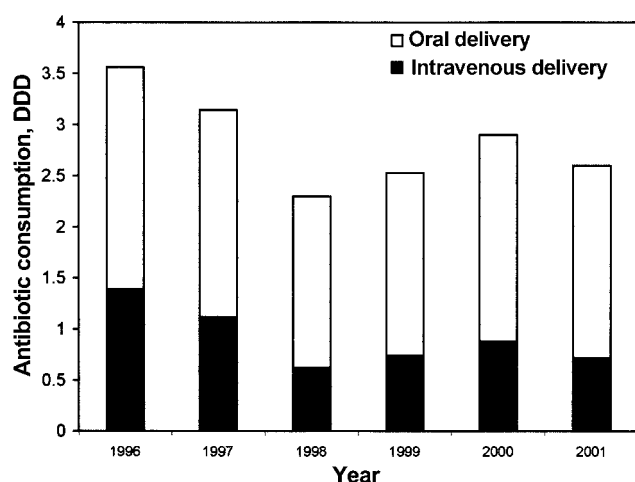
h per year for the whole medical staff. The theoretical costs for these hours can be calculated to ~US\$20,000 for development and implementation and to ~US\$20,000 per year for maintenance.

**Long-term effect of the program.** Compared with 1996 (the last full year before the intervention), average total DDDs per patient admitted to the Department of Internal Medicine were down 35% in 1998 (the first full year with intervention), and they were down 26% in 2001 (figure 1). Average intravenous DDDs were down 55% and 48%, and average oral DDDs 23% and 13% in the corresponding time period. Average antibiotic drug costs per patient admitted to the medical wards and to the ICU decreased by 51% and 50%, respectively, between 1996 and 1998 (figure 2). Costs remained fairly stable during the next few years (decreases in 2001 of 46% and 39%, respectively, compared with 1996).

Susceptibility patterns of bacterial organisms showed a slightly favorable trend toward some broad-spectrum antibiotics (table 6), but the small numbers do not permit any definitive conclusions to be drawn.

## DISCUSSION

This study demonstrates that an easily applicable and inexpensive multifaceted intervention program was highly effective in reducing the number and costs of antibiotics prescribed. Average cost savings per patient admitted amounted to US\$100,



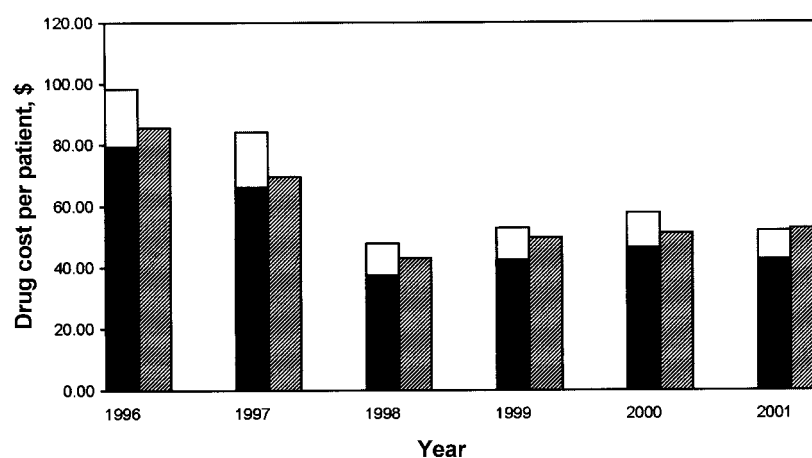
**Figure 1.** Bar graph illustrating antibiotic consumption in defined daily doses (DDD) per patient admitted to the medical department (not including intensive care unit admissions) 1996–2001. The last year before intervention measures was 1996, and 1998 was the first year that the intervention program was fully introduced.

resulting in projected annual savings for our medical department in the amount of US\$200,000. The program did not unfavorably affect overall mortality, infection-related mortality, or relapse rates for serious infections. We could demonstrate a persistence of the program's effectiveness over a 4-year observation period. The 2 most important factors leading to cost savings were a reduction in the use of unnecessary antibiotic treatments and a more diligent use of expensive intravenous broad-spectrum antibiotics.

Our study has several limitations. First, this was not a randomized trial, which would have been difficult to perform

within a single department because of knowledge contamination between groups. However, physicians were unaware that this study was performed, which allowed us to test the effect of the program on the treatment behavior of the same physicians in a real-world setting. Second, we did not evaluate the individual physicians' compliance with the implemented guidelines with a formal peer-review process. Third, we cannot exclude with certainty that the decrease in the number of antibiotic treatment courses was the result of an underlying decrease in the number of infections and in the patients' need for antibiotic treatment. Our analyses of indicators for disease severity revealed no decrease of severe infections during the intervention period. However, there was a substantial reduction in the number of antibiotic prescriptions for certain conditions, such as upper respiratory tract infections. We interpret this change not as a shift of the infectious disease pattern but as the result of a more critical use of antibiotics and as one consequence of our intervention program. The long-term development of antibiotic expenditures, with a steady increase from 1992 until 1996 (data not shown), and the sharp and sustained decrease after the intervention additionally point to a more critical use of antibiotics as the likely reason for the decrease of treatments. Fourth, postdischarge follow-up was restricted to the evaluation of the need for rehospitalization. Thus, we cannot exclude the notion that, after the intervention, the outcome of antibiotic treatment was different for patients who were not in need of rehospitalization. Fifth, we limited the long-term follow-up to antibiotic consumption and costs without further controlling for treatment outcomes by chart review.

The study has several strengths: the short-term analysis of the intervention program is based on individual patient data extracted in great detail directly from the medical charts. This



**Figure 2.** Bar graph illustrating antibiotic drug costs per patient admitted to the medical department (black bars, costs for intravenous antibiotics; white bars, costs for oral antibiotics) and to the intensive care unit (hatched bars, costs for intravenous plus oral antibiotics) for 1996–2001. The last year before intervention measures was 1996, and 1998 was the first year that the intervention program was fully introduced.

**Table 6. Resistance patterns of selected bacterial organisms toward 6 antibiotics during 1996–2001.**

| Organism                      | Percentage of resistant or intermediately resistant organisms, by drug |                     |             |                         |                         |            |
|-------------------------------|--|---------------------|-------------|-------------------------|-------------------------|------------|
|                               | Ciprofloxacin  | Imipenem-cilastatin | Ceftazidime | Piperacillin-tazobactam | Amoxicillin-clavulanate | Cefuroxime |
| <i>Escherichia coli</i>       |  |                     |             |                         |                         |            |
| 1996                          | 1  | 0                   | 0           | 2                       | 26                      | 3          |
| 1997                          | 1  | 0                   | 0           | 2                       | 26                      | 2          |
| 1998                          | 3  | 1                   | 0           | 2                       | 23                      | 3          |
| 1999                          | 1  | 0                   | 0           | 1                       | 27                      | 2          |
| 2000                          | 2  | 0                   | 0           | NT                      | 18                      | 2          |
| 2001                          | 3  | 0                   | 0           | NT                      | 22                      | 1          |
| <i>Klebsiella pneumoniae</i>  |  |                     |             |                         |                         |            |
| 1996                          | 11   | 0                   | 0           | 15                      | 16                      | 11         |
| 1997                          | 0  | 0                   | 0           | 17                      | 7                       | 7          |
| 1998                          | 7  | 0                   | 0           | 0                       | 0                       | 0          |
| 1999                          | 0  | 0                   | 0           | 0                       | 7                       | 3          |
| 2000                          | 0  | 0                   | 0           | NT                      | 13                      | 0          |
| 2001                          | 0  | 0                   | 0           | NT                      | 18                      | 0          |
| <i>Pseudomonas aeruginosa</i> |  |                     |             |                         |                         |            |
| 1996                          | 15   | 15                  | 9           | 6                       | NT                      | NT         |
| 1997                          | 10   | 27                  | 5           | 0                       | NT                      | NT         |
| 1998                          | 27   | 15                  | 4           | 0                       | NT                      | NT         |
| 1999                          | 13   | 4                   | 0           | 0                       | NT                      | NT         |
| 2000                          | 9  | 13                  | 17          | NT                      | NT                      | NT         |
| 2001                          | 5  | 16                  | 0           | NT                      | NT                      | NT         |
| <i>Staphylococcus aureus</i>  |  |                     |             |                         |                         |            |
| 1996                          | NT   | NT                  | NT          | NT                      | 0                       | 0          |
| 1997                          | NT   | NT                  | NT          | NT                      | 0                       | 0          |
| 1998                          | NT   | NT                  | NT          | NT                      | 0                       | 2          |
| 1999                          | NT   | NT                  | NT          | NT                      | 0                       | 0          |
| 2000                          | NT   | NT                  | NT          | NT                      | 7                       | 7          |
| 2001                          | NT   | NT                  | NT          | NT                      | 0                       | 0          |
| <i>Enterococcus</i> species   |  |                     |             |                         |                         |            |
| 1996                          | NT   | NT                  | NT          | NT                      | 0                       | NT         |
| 1997                          | NT   | NT                  | NT          | NT                      | 0                       | NT         |
| 1998                          | NT   | NT                  | NT          | NT                      | 0                       | NT         |
| 1999                          | NT   | NT                  | NT          | NT                      | 0                       | NT         |
| 2000                          | NT   | NT                  | NT          | NT                      | 2                       | NT         |
| 2001                          | NT   | NT                  | NT          | NT                      | 6                       | NT         |

**NOTE.** The year that the intervention program was fully introduced was 1998. NT, not tested.

allowed us to make very precise cost calculations, and to analyze in detail the behavior changes of the physicians and the main reasons for the cost reduction observed after the multifaceted intervention. Second, all patients admitted were included, and the follow-up regarding the need for a rehospitalization was complete for all patients. Third, the follow-up period was long; most studies document follow-up periods of <1 year [12, 13, 19, 22] or of 1–2 years [3, 10, 11, 18, 20, 21]. Only 1 study,

which evaluated a computer-assisted decision-support program, documented a favorable long-term effect over 7 years [15].

Apart from avoiding unnecessary antibiotic treatments and a more diligent use of expensive broad-spectrum antibiotics, a priori oral delivery, and early switching from the intravenous to the oral route of administration are recognized as important cost-lowering strategies in the literature [9]. In our study, we



observed only a marginal difference associated with these factors, which was probably because good performance was already in place before the intervention.

DDDs and calculated costs per admitted and treated patient or per hospital and treatment day were rather low, compared with other studies [10, 11, 13, 15, 17, 18, 20, 22, 24]. However, comparison with these studies is limited as a result of differences in settings, inclusion in these studies of nonmedical patients, and different case mix. The same holds true for direct comparisons of costs, which are further flawed by price differences and general differences of health cost structures between countries.

The acute and sustained cost reduction achieved by our intervention program is substantial. Remarkably, it was attained in a setting with a rapidly changing medical staff that consists, in large part, of physician-trainees. In addition, it was achieved not by computer assistance, but by combining several methods under the responsibility of one person—probably the most important factor for the long-lasting success. Such a strategy may be more feasible in smaller community hospitals and single departments where sophisticated computer aids may not be readily available. The generalizability of our findings to larger medical departments with a different case mix—for example, university hospitals—may be limited, however. In such settings, or in countries with higher expenditures for hospital staff, costs for such an intervention program could be greater and consequently savings smaller than in the present study. Similarly, unlike at our hospital, in other settings or countries, including United States hospitals, the implementation and maintenance of such an antibiotic-management program may not be feasible without additional monetary support of the staff by hospital administration.

In summary, in a medical department at a community hospital, an inexpensive comprehensive intervention program aimed at reducing expenditures for antibiotic treatment proved to be highly successful in the short and long term and can be a reasonable means for cost containment in similar settings.

## Acknowledgments

We thank Christian Conrad from the Division of Infection Control of our hospital for providing us with bacterial susceptibility patterns. We thank Sonia Gonzalez for secretarial assistance.

## References

- Avorn J, Soumerai SB, Taylor W, et al. Reduction of incorrect antibiotic dosing through a structured educational order form. *Arch Intern Med* 1988; 148:1720–4.
- Baum C, Kennedy DK, Knapp DE, et al. Drug utilization in the United States, 1985. DHHS. Rockville, MD: US Food and Drug Administration/National Center for Drugs and Biologics, 1986.
- Salama S, Roststein C, Mandell L. A multi-disciplinary hospital-based antimicrobial use program: impact on hospital pharmacy expenditures and drug use. *Can J Infect Dis* 1996; 7:104–9.
- Reimann HA. The misuse of antibiotics. *Med Clin North Am* 1961; 45:849–54.
- Marr JJ, Moffet HL, Kunin CM. Guidelines for improving the use of antimicrobial agents in hospitals: a statement by the Infectious Diseases Society of America. *J Infect Dis* 1988; 157:869–76.
- Kislak JW, Eickhoff TC, Finland M. Hospital-acquired infections and antibiotic usage in the Boston City Hospital—January, 1964. *N Engl J Med* 1964; 271:834–5.
- Cohen ML. Epidemiology of drug resistance: implications for a post-antimicrobial era. *Science* 1992; 257:1050–5.
- Duncan RA. Controlling use of antimicrobial agents. *Infect Control Hosp Epidemiol* 1997; 18:260–6.
- John JF Jr, Fishman NO. Programmatic role of the infectious diseases physician in controlling antimicrobial costs in the hospital. *Clin Infect Dis* 1997; 24:471–85.
- Coleman RW, Rodondi LC, Kaubisch S, et al. Cost-effectiveness of prospective and continuous parenteral antibiotic control: experience at the Palo Alto Veterans Affairs Medical Center from 1987 to 1989. *Am J Med* 1991; 90:439–44.
- Woodward RS, Medoff G, Smith MD, Gray JL. Antibiotic cost savings from formulary restrictions and physician monitoring in a medical-school-affiliated hospital. *Am J Med* 1987; 83:817–23.
- Maswoswe JJ, Okpara AU. Enforcing a policy for restricting antimicrobial drug use. *Am J Health Syst Pharm* 1995; 52:1433–5.
- Briceland LL, Nightingale CH, Quintiliani R, et al. Antibiotic streamlining from combination therapy to monotherapy utilizing an interdisciplinary approach. *Arch Intern Med* 1988; 148:2019–22.
- Evans RS, Classen DC, Pestotnik SL, et al. Improving empiric antibiotic selection using computer decision support. *Arch Intern Med* 1994; 154:878–84.
- Pestotnik SL, Classen DC, Evans RS, Burke JP. Implementing antibiotic practice guidelines through computer-assisted decision support: clinical and financial outcomes. *Ann Intern Med* 1996; 124:884–90.
- Solomon DH, Van Houten L, Glynn RJ, et al. Academic detailing to improve use of broad-spectrum antibiotics at an academic medical center. *Arch Intern Med* 2001; 161:1897–902.
- Fletcher CV, Metzler D, Borchardt-Phelps P, Rodman JH. Patterns of antibiotic use and expenditures during 7 years at a university hospital. *Pharmacotherapy* 1990; 10:199–204.
- Hirschmann SZ, Meyers BR, Bradbury K, et al. Use of antimicrobial agents in a university teaching hospital. *Arch Intern Med* 1988; 148:2001–7.
- Gross R, Morgan AS, Kinky DE, et al. Impact of a hospital-based antimicrobial management program on clinical and economic outcomes. *Clin Infect Dis* 2001; 33:289–95.
- Carling PC, Fung T, Coldiron JS. Parenteral antibiotic use in acute-care hospitals: a standardized analysis of fourteen institutions. *Clin Infect Dis* 1999; 29:1189–96.
- Schentag JJ, Ballou CH, Fritz AL, et al. Changes in antimicrobial agent usage resulting from interactions among clinical pharmacy, the infectious disease division, and the microbiology laboratory. *Diagn Microbiol Infect Dis* 1993; 16:255–64.
- Fraser GL, Stogsdill P, Dickens JD Jr, et al. An evaluation of patient safety and economic outcomes. *Arch Intern Med* 1997; 157:1689–94.
- Maxwell M, Heaney D, Howie JGR, Noble S. General practice fundholding: observations on prescribing patterns and costs using the defined daily dose method. *BMJ* 1993; 307:1190–4.
- Von Gunten V, Reymond J-F, Troillet N. Use of broad-spectrum antibiotics in six non-university Swiss hospitals. *Swiss Med Wkly* 2001; 131:438–41.